

SEQUENCE LISTING

<110> Bayer Corporation

<120> Protein Having Activity As An Angiogenesis Modulator

<130> MSB-7265-PCT

<140> PCT/US 01/10222

<141> 2001-03-30

<150> US 60/266,300

<151> 2000-03-31

<160> 34

<170> PatentIn version 3.1

<210> 1

<211> 208

<212> PRT

<213> Homo sapiens

<400> 1

Gln Val His Gly Gly Phe Ser Gln Trp Ser Ala Trp Arg Ala Cys Ser 1 5 10 15

Val Thr Cys Gly Lys Gly Ile Gln Lys Arg Ser Arg Leu Cys Asn Gln 20 25 30

Pro Leu Pro Ala Asn Gly Gly Lys Pro Cys Gln Gly Ser Asp Leu Glu 35 40 45

Met Arg Asn Cys Gln Asn Lys Pro Cys Pro Val Asp Gly Ser Trp Ser 50 55 60

Glu Trp Ser Leu Trp Glu Glu Cys Thr Arg Ser Cys Gly Arg Gly Asn 65 70 75 80

Gln Thr Arg Thr Arg Thr Cys Asn Asn Pro Ser Val Gln His Gly Gly 85 90 95

Arg Pro Cys Glu Gly Asn Ala Val Glu Ile Ile Met Cys Asn Ile Arg 100 105 110

Pro Cys Pro Val His Gly Ala Trp Ser Ala Trp Gln Pro Trp Gly Thr
115 120 125

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Cys Ser Glu Ser Cys Gly Lys Gly Thr Gln Thr Arg Ala Arg Leu Cys
                        135
Asn Asn Pro Pro Pro Ala Phe Gly Gly Ser Tyr Cys Asp Gly Ala Glu
145
                    150
                                        155
Thr Gln Met Gln Val Cys Asn Glu Arg Asn Cys Pro Ile His Gly Lys
                165
                                    170
Trp Ala Thr Trp Ala Ser Trp Ser Ala Cys Ser Val Ser Cys Gly Gly
            180
                                185
Gly Ala Arg Gln Arg Thr Arg Gly Cys Ser Asp Pro Val Pro Gln Tyr
        195
                            200
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Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Ala Asn Pro Gln Leu
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                                                        15
Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu
Arg Asp Asn Gln Leu Val Val Glu Gly Leu Tyr Leu Ile Tyr Ser Gln
                            40
Val Leu Phe
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<400> 3
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Arg Ala Pro Phe Lys Lys Ser Trp Ala Tyr Leu Gln Val Ala Lys His

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1 5 10 15

Lys Leu Ser Trp Asn Lys Asp Gly Ile Leu His Gly Val Arg Tyr Gln Asp Gly Asn Leu Val Ile Gln Phe Pro Gly Leu Tyr Phe Ile Ile Cys 40 Gln Leu Gln Phe 50 <210> 4 <211> 8 <212> PRT <213> Artificial Sequence <220> <223> FLAG sequence for expressed protein <400> 4 Asp Tyr Lys Asp Asp Asp Lys <210> 5 <211> 6 <212> PRT <213> Artificial Sequence <220> <223> Sequence with antineoangiogenic activity <400> 5 Cys Ser Val Thr Cys Gly 5 <210> 6 <211> 50 <212> PRT <213> Artificial Sequence <220> Isolated type 1 thrombospondin domain sequence <223> <400> 6

Asp Gly Trp Ser Pro Trp Ser Glu Trp Thr Ser Cys Ser Thr Ser Cys

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Gly Asn Gly Ile Gln Gln Arg Gly Arg Ser Cys Asp Ser Leu Asn Asn Arg Cys Glu Gly Ser Ser Val Gln Thr Arg Thr Cys His Ile Gln Glu Cys Asp 50 <210> 7 <211> 55 <212> PRT <213> Artificial Sequence <220> <223> Isolated type 1 thrombospondin domain sequence <400> 7 Gly Gly Trp Ser His Trp Ser Pro Trp Ser Ser Cys Ser Val Thr Cys 5 10 Gly Asp Gly Val Ile Thr Arg Ile Arg Leu Cys Asn Ser Pro Ser Pro 20 Gln Met Asn Gly Lys Pro Cys Glu Gly Glu Ala Arg Glu Thr Lys Ala 35 40 Cys Lys Lys Asp Ala Cys Pro 50 <210> 8 <211> 55 <212> PRT <213> Artificial Sequence <220> <223> Isolated type 1 thrombospondin domain sequence <400> 8 Gly Gly Trp Gly Pro Trp Ser Pro Trp Asp Ile Cys Ser Val Thr Cys 5

Gln Phe Gly Gly Lys Asp Cys Val Gly Asp Val Thr Glu Asn Gln Ile

Gly Gly Gly Val Gln Lys Arg Ser Arg Leu Cys Asn Asn Pro Thr Pro

35 40 45

Cys Asn Lys Gln Asp Cys Pro 50 55

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<210> 9

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<400> 9

Glu Gly Trp Ser Pro Trp Ala Glu Trp Thr Gln Cys Ser Val Thr Cys
1 5 10 15

Gly Ser Gly Thr Gln Gln Arg Gly Arg Ser Cys Asp Val Thr Ser Asn 20 25 30

Thr Cys Leu Gly Pro Ser Ile Gln Thr Arg Ala Cys Ser Leu Ser Lys 35 40 45

Cys Asp 50

<210> 10

<211> 55

<212> PRT

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<223> Isolated type 1 thrombospondin domain sequence

<400> 10

Gly Gly Trp Ser His Trp Ser Pro Trp Ser Ser Cys Ser Val Thr Cys 1 5 10 15

Gly Val Gly Asn Ile Thr Arg Ile Arg Leu Cys Asn Ser Pro Val Pro 20 25 30

Gln Met Gly Gly Lys Asn Cys Lys Gly Ser Gly Arg Glu Thr Lys Ala 35 40 45

Cys Gln Gly Ala Pro Cys Pro 50 55

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<210> 11
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Gly Arg Trp Ser Pro Trp Ser Pro Trp Ser Ala Cys Thr Val Thr Cys
Ala Gly Gly Ile Arg Glu Arg Thr Arg Val Cys Asn Ser Pro Glu Pro
Gln Tyr Gly Gly Lys Ala Cys Val Gly Asp Val Gln Glu Arg Gln Met
                            40
Cys Asn Lys Arg Ser Cys Pro
<210> 12
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Gly Gly Trp Lys Leu Trp Ser Leu Trp Gly Glu Cys Thr Arg Asp Cys
Gly Gly Gly Leu Gln Thr Arg Thr Arg Thr Cys Leu Pro Ala Pro Gly
            20
                                25
Val Glu Gly Gly Cys Glu Gly Val Leu Glu Glu Gly Arg Gln Cys
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                            40
Asn Arg Glu Ala Cys Gly
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<210> 13
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Pro Ala Ala Glu Glu Trp Ser Pro Trp Ser Val Cys Ser Ser Thr Cys
Gly Glu Gly Trp Gln Thr Arg Thr Arg Phe Cys Val Ser Ser Ser Tyr
                                25
Ser Thr Gln Cys Ser Gly Pro Leu Arg Glu Gln Arg Leu Cys Asn Asn
                            40
Ser Ala Val Cys Pro
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Gly Ala Trp Asp Glu Trp Ser Pro Trp Ser Leu Cys Ser Ser Thr Cys
Gly Arg Gly Phe Arg Asp Arg Thr Arg Thr Cys Arg Pro Pro Gln Phe
            20
Gly Gly Asn Pro Cys Glu Gly Pro Glu Lys Gln Thr Lys Phe Cys Asn
        35
Ile Ala Leu Cys Pro
    50
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<400> 15
Gly Asn Trp Asn Glu Trp Ser Ser Trp Ser Ala Cys Ser Ala Ser Cys
                                    10
Ser Gln Gly Arg Gln Gln Arg Thr Arg Glu Cys Asn Gly Pro Ser Tyr
Gly Gly Ala Glu Cys Gln Gly His Trp Val Glu Thr Arg Asp Cys Phe
Leu Gln Gln Cys Pro
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<210> 16
<211> 53
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<400> 16
Gly Lys Trp Gln Ala Trp Ala Ser Trp Gly Ser Cys Ser Val Thr Cys
               5
Gly Ala Gly Ser Gln Arg Arg Glu Arg Val Cys Ser Gly Pro Phe Phe
Gly Gly Ala Ala Cys Gln Gly Pro Gln Asp Glu Tyr Arg Gln Cys Gly
                           40
Thr Gln Arg Cys Pro
   50
<210> 17
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Pro Ala Ala Glu Glu Trp Ser Pro Trp Ser Val Cys Ser Leu Thr Cys

<400> 17

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Gly Gln Gly Leu Gln Val Arg Thr Arg Ser Cys Val Ser Ser Pro Tyr
Gly Thr Leu Cys Ser Gly Pro Leu Arg Glu Thr Arg Pro Cys Asn Asn
                            40
Ser Ala Thr Cys Pro
    50
<210> 18
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      Isolated type 1 thrombospondin domain sequence
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Gly Val Trp Glu Glu Trp Gly Ser Trp Ser Leu Cys Ser Arg Ser Cys
Gly Arg Gly Ser Arg Ser Arg Met Arg Thr Cys Val Pro Pro Gln His
                                25
Gly Gly Lys Ala Cys Glu Gly Pro Glu Leu Gln Thr Lys Leu Cys Ser
        35
                            40
Met Ala Ala Cys Pro
    50
<210> 19
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<212> PRT
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<400> 19
Gly Gln Trp Leu Glu Trp Gly Pro Trp Gly Pro Cys Ser Thr Ser Cys
Ala Asn Gly Thr Gln Gln Arg Ser Arg Lys Cys Ser Val Ala Gly Pro
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25

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Ala Trp Ala Thr Cys Thr Gly Ala Leu Thr Asp Thr Arg Glu Cys Ser
Asn Leu Glu Cys Pro
    50
<210> 20
<211> 53
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<213> Artificial Sequence
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<400> 20
Ser Lys Trp Gly Pro Trp Asn Ala Trp Ser Leu Cys Ser Lys Thr Cys
                                    10
Asp Thr Gly Trp Gln Arg Arg Phe Arg Met Cys Gln Ala Thr Gly Thr
            20
                                25
Gln Gly Tyr Pro Cys Glu Gly Thr Gly Glu Glu Val Lys Pro Cys Ser
Glu Lys Arg Cys Pro
    50
<210> 21
<211> 52
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<213> Artificial Sequence
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<223> Isolated type 1 thrombospondin domain sequence
<400> 21
Ser Gly Val Glu Glu Trp Ser Gln Trp Ser Thr Cys Ser Val Thr Cys
                5
                                    10
Gly Gln Gly Ser Gln Val Arg Thr Arg Thr Cys Val Ser Pro Tyr Gly
            20
                                25
                                                    30
Thr His Cys Ser Gly Pro Leu Arg Glu Ser Arg Val Cys Asn Asn Thr
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Ala Leu Cys Pro

<210> 24 <211> 53

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<210> 22
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<400> 22
Gly Val Trp Glu Glu Trp Ser Pro Trp Ser Leu Cys Ser Phe Thr Cys
                                   10
Gly Arg Gly Gln Arg Thr Arg Thr Arg Ser Cys Thr Pro Pro Gln Tyr
            20
                                25
Gly Gly Arg Pro Cys Glu Gly Pro Glu Thr His His Lys Pro Cys Asn
Ile Ala Leu Cys Pro
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<210> 23
<211> 53
<212> PRT
<213> Artificial Sequence
<223> Isolated type 1 thrombospondin domain sequence
<400> 23
Gly Gln Trp Gln Glu Trp Ser Ser Trp Ser Gln Cys Ser Val Thr Cys
               5
                                                        15
Ser Asn Gly Thr Gln Gln Arg Ser Arg Gln Cys Thr Ala Ala Ala His
            20
Gly Gly Ser Glu Cys Arg Gly Pro Trp Ala Glu Ser Arg Glu Cys Tyr
Asn Pro Glu Cys Thr
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<212> PRT
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<400> 24
Gly Gln Trp Asn Gln Trp Gly His Trp Ser Gly Cys Ser Lys Ser Cys
                5
                                    10
Asp Gly Gly Trp Glu Arg Arg Ile Arg Thr Cys Gln Gly Ala Val Ile
Thr Gly Gln Gln Cys Glu Gly Thr Gly Glu Glu Val Arg Arg Cys Ser
                            40
Glu Gln Arg Cys Pro
    50
<210> 25
<211> 55
<212> PRT
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<223>
<400> 25
Gly Gly Phe Ser Gln Trp Ser Ala Trp Arg Ala Cys Ser Val Thr Cys
                5
Gly Lys Gly Ile Gln Lys Arg Ser Arg Leu Cys Asn Gln Pro Leu Pro
Ala Asn Gly Gly Lys Pro Cys Gln Gly Ser Asp Leu Glu Met Arg Asn
        35
                            40
Cys Gln Asn Lys Pro Cys Pro
   50
                        55
<210> 26
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<400> 26
Gly Ser Trp Ser Glu Trp Ser Leu Trp Glu Glu Cys Thr Arg Ser Cys
Gly Arg Gly Asn Gln Thr Arg Thr Arg Thr Cys Asn Asn Pro Ser Val
            20
                                25
Gln His Gly Gly Arg Pro Cys Glu Gly Asn Ala Val Glu Ile Ile Met
                            40
Cys Asn Ile Arg Pro Cys Pro
<210> 27
<211> 55
<212> PRT
<213> Artificial Sequence
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<400> 27
Gly Ala Trp Ser Ala Trp Gln Pro Trp Gly Thr Cys Ser Glu Ser Cys
Gly Lys Gly Thr Gln Thr Arg Ala Arg Leu Cys Asn Asn Pro Pro Pro
            20
                                25
Ala Phe Gly Gly Ser Tyr Cys Asp Gly Ala Glu Thr Gln Met Gln Val
       35
                            40
Cys Asn Glu Arg Asn Cys Pro
    50
<210> 28
<211> 55
<212> PRT
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Isolated type 1 thrombospondin domain sequence

Gly Lys Trp Ala Thr Trp Ala Ser Trp Ser Ala Cys Ser Val Ser Cys

<223>

<400> 28

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Gly Gly Gly Ala Arg Gln Arg Thr Arg Gly Cys Ser Asp Pro Val Pro
                               25
Gln Tyr Gly Gly Arg Lys Cys Glu Gly Ser Asp Val Gln Ser Asp Phe
Cys Asn Ser Asp Pro Cys Pro
<210> 29
<211> 55
<212> PRT
<213> Artificial Sequence
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<223> Isolated type 1 thrombospondin domain sequence
<400> 29
Gly Asn Trp Ser Pro Trp Ser Gly Trp Gly Thr Cys Ser Arg Thr Cys
Asn Gly Gly Gln Met Arg Arg Tyr Arg Thr Cys Asp Asn Pro Pro Pro
           20
                               25
Ser Asn Gly Gly Arg Ala Cys Gly Gly Pro Asp Ser Gln Ile Gln Arg
                           40
Cys Asn Thr Asp Met Cys Pro
<210> 30
<211> 55
<212> PRT
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<400> 30
Gly Ser Trp Gly Ser Trp His Ser Trp Ser Gln Cys Ser Ala Ser Cys
               5
Gly Gly Glu Lys Thr Arg Lys Arg Leu Cys Asp His Pro Val Pro
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Val Lys Gly Gly Arg Pro Cys Pro Gly Asp Thr Thr Gln Val Thr Arg
35 40 45

Cys Asn Val Gln Ala Cys Pro 50 55

<210> 31

<211> 197

<212> PRT

<213> Homo sapiens

<400> 31

Gln Trp Ser Ala Trp Arg Ala Cys Ser Val Thr Cys Gly Lys Gly Ile 1 5 10 15

Gln Lys Arg Ser Arg Leu Cys Asn Gln Pro Leu Pro Ala Asn Gly Gly
20 25 30

Lys Pro Cys Gln Gly Ser Asp Leu Glu Met Arg Asn Cys Gln Asn Lys 35 40 45

Pro Cys Pro Val Asp Gly Ser Trp Ser Glu Trp Ser Leu Trp Glu Glu 50 55 60

Cys Thr Arg Ser Cys Gly Arg Gly Asn Gln Thr Arg Thr Arg Thr Cys 70 75 80

Asn Asn Pro Ser Val Gln His Gly Gly Arg Pro Cys Glu Gly Asn Ala 85 90 95

Val Glu Ile Ile Met Cys Asn Ile Arg Pro Cys Pro Val His Gly Ala 100 105 110

Trp Ser Ala Trp Gln Pro Trp Gly Thr Cys Ser Glu Ser Cys Gly Lys
115 120 125

Gly Thr Gln Thr Arg Ala Arg Leu Cys Asn Asn Pro Pro Pro Ala Phe 130 135 140

Gly Gly Ser Tyr Cys Asp Gly Ala Glu Thr Gln Met Gln Val Cys Asn 145 150 155 160

Glu Arg Asn Cys Pro Ile His Gly Lys Trp Ala Thr Trp Ala Ser Trp

165 170 175

Ser Ala Cys Ser Val Ser Cys Gly Gly Gly Ala Arg Gln Arg Thr Arg 180 185 190

Gly Cys Ser Asp Pro 195

<210> 32

<211> 194

<212> PRT

<213> Homo sapiens

<400> 32

Glu Trp Ser Pro Trp Ser Val Cys Ser Ser Thr Cys Gly Glu Gly Trp

5 10 15

Gln Thr Arg Thr Arg Phe Cys Val Ser Ser Ser Tyr Ser Thr Gln Cys
20 25 30

Ser Gly Pro Leu Arg Glu Gln Arg Leu Cys Asn Asn Ser Ala Val Cys 35 40 45

Pro Val His Gly Ala Trp Asp Glu Trp Ser Pro Trp Ser Leu Cys Ser 50 55 60

Ser Thr Cys Gly Arg Gly Phe Arg Asp Arg Thr Arg Thr Cys Arg Pro 65 70 75 80

Pro Gln Phe Gly Gly Asn Pro Cys Glu Gly Pro Glu Lys Gln Thr Lys 85 90 95

Phe Cys Asn Ile Ala Leu Cys Pro Gly Arg Ala Val Asp Gly Asn Trp
100 105 110

Asn Glu Trp Ser Ser Trp Ser Ala Cys Ser Ala Ser Cys Ser Gln Gly
115 120 125

Arg Gln Gln Arg Thr Arg Glu Cys Asn Gly Pro Ser Tyr Gly Gly Ala 130 135 140

Glu Cys Gln Gly His Trp Val Glu Thr Arg Asp Cys Phe Leu Gln Gln 145 150 155 160

Cys Pro Val Asp Gly Lys Trp Gln Ala Trp Ala Ser Trp Gly Ser Cys 165 170 175

Ser Val Thr Cys Gly Ala Gly Ser Gln Arg Arg Glu Arg Val Cys Ser 180 185 190

Gly Pro

<210> 33

<211> 1336

<212> PRT

<213> Homo sapiens

<400> 33

Thr Pro Ile Gly Arg Pro Arg Ile Arg His Gln Asp Lys Arg Thr Val 1 5 10 15

Asp Leu Thr Val Gln Val Pro Pro Ser Ile Ala Asp Glu Pro Thr Asp 20 25 30

Phe Leu Val Thr Lys His Ala Pro Ala Val Ile Thr Cys Thr Ala Ser

Gly Val Pro Phe Pro Ser Ile His Trp Thr Lys Asn Gly Ile Arg Leu
50 60

Leu Pro Arg Gly Asp Gly Tyr Arg Ile Leu Ser Ser Gly Ala Ile Glu 65 70 75 80

Ile Leu Ala Thr Gln Leu Asn His Ala Gly Arg Tyr Thr Cys Val Ala 85 90 95

Arg Asn Ala Ala Gly Ser Ala His Arg His Val Thr Leu His Val His
100 105 110

Glu Pro Pro Val Ile Gln Pro Gln Pro Ser Glu Leu His Val Ile Leu 115 120 125

Asn Asn Pro Ile Leu Leu Pro Cys Glu Ala Thr Gly Thr Pro Ser Pro 130 135 140

Phe Ile Thr Trp Gln Lys Glu Gly Ile Asn Val Asn Thr Ser Gly Arg

145 150 155 160

Asn His Ala Val Leu Pro Ser Gly Gly Leu Gln Ile Ser Arg Ala Val 165 170 175

Arg Glu Asp Ala Gly Thr Tyr Met Cys Val Ala Gln Asn Pro Ala Gly
180 185 190

Thr Ala Leu Gly Lys Ile Lys Leu Asn Val Gln Val Pro Pro Val Ile 195 200 205

Ser Pro His Leu Lys Glu Tyr Val Ile Ala Val Asp Lys Pro Ile Thr 210 215 220

Leu Ser Cys Glu Ala Asp Gly Leu Pro Pro Pro Asp Ile Thr Trp His 225 230 235 240

Lys Asp Gly Arg Ala Ile Val Glu Ser Ile Arg Gln Arg Val Leu Ser 245 250 255

Ser Gly Ser Leu Gln Ile Ala Phe Val Gln Pro Gly Asp Ala Gly His 260 265 270

Tyr Thr Cys Met Ala Ala Asn Val Ala Gly Ser Ser Ser Thr Ser Thr 275 280 285

Lys Leu Thr Val His Val Pro Pro Arg Ile Arg Ser Thr Lys Gly His 290 295 300

Tyr Thr Val Asn Glu Asn Ser Gln Ala Ile Leu Pro Cys Val Ala Asp 305 310 315 320

Gly Ile Pro Thr Pro Ala Ile Asn Trp Lys Lys Asp Asn Val Leu Leu 325 330 335

Ala Asn Leu Leu Gly Lys Tyr Thr Ala Glu Pro Tyr Gly Glu Leu Ile 340 345 350

Leu Glu Asn Val Val Leu Glu Asp Ser Gly Phe Tyr Thr Cys Val Ala 355 360 365

Asn Asn Ala Ala Gly Glu Asp Thr His Thr Val Ser Leu Thr Val His 370 375 380

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Gly	Glu	Gln	Leu	Arg 405	Leu	Ser	Сув	Lys	Ala 410	Thr	Gly	Ile	Pro	Leu 415	Pro
Lys	Leu	Thr	Trp 420	Thr	Phe	Asn	Asn	Asn 425	Ile	Ile	Pro	Ala	His 430	Phe	Asp
Ser	Val	Asn 435	Gly	His	Ser	Glu	Leu 440	Val	Ile	Glu	Arg	Val 445	Ser	Lys	Glu
Asp	Ser 450	Gly	Thr	Tyr	Val	Cys 455	Thr	Ala	Glu	Asn	Ser 460	Val	Gly	Phe	Val
Lys 465	Ala	Ile	Gly	Phe	Val 470	Tyr	Val	Lys	Glu	Pro 475	Pro	Val	Phe	Lys	Gly 480
Asp	Tyr	Pro	Ser	Asn 485	Trp	Ile	Glu	Pro	Leu 490	Gly	Gly	Asn	Ala	Ile 495	Leu
Asn	Cys	Glu	Val 500	Lys	Gly	Asp	Pro	Thr 505	Pro	Thr	Ile	Gln	Trp 510	Asn	Arg
Lys	Gly	Val 515	Asp	Ile	Glu	Ile	Ser 520	His	Arg	Ile	Arg	Gln 525	Leu	Gly	Asn
	Ser 530	Leu	Ala	Ile	Tyr	Gly 535	Thr	Val	Asn	Glu	Asp 540	Ala	Gly	Asp	Tyr
Thr 545	Cys	Val	Ala	Thr	Asn 550	Glu	Ala	Gly	Val	Val 555	Glu	Arg	Ser	Met	Ser 560
Leu	Thr	Leu	Arg	Ser 565	Pro	Pro	Ile	Ile	Thr 570	Leu	Glu	Pro	Val	Glu 575	Thr
Val	Ile	Asn	Ala 580	Gly	Gly	Lys	Ile	Ile 585	Leu	Asn	Cys	Gln	Ala 590	Thr	Gly
Glu	Pro	Gln 595	Pro	Thr	Ile	Thr	Trp 600	Ser	Arg	Gln	Gly	His 605	Ser	Ile	Ser

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Trp Asp Asp Arg Val Asn Val Leu Ser Asn Asn Ser Leu Tyr Ile Ala Asp Ala Gln Lys Glu Asp Thr Ser Glu Phe Glu Cys Val Ala Arg Asn Leu Met Gly Ser Val Leu Val Arg Val Pro Val Ile Val Gln Val His Gly Gly Phe Ser Gln Trp Ser Ala Trp Arg Ala Cys Ser Val Thr Cys Gly Lys Gly Ile Gln Lys Arg Ser Arg Leu Cys Asn Gln Pro Leu Pro Ala Asn Gly Gly Lys Pro Cys Gln Gly Ser Asp Leu Glu Met Arg Asn Cys Gln Asn Lys Pro Cys Pro Val Asp Gly Ser Trp Ser Glu Trp Ser Leu Trp Glu Glu Cys Thr Arg Ser Cys Gly Arg Gly Asn Gln Thr Arg Thr Arg Thr Cys Asn Asn Pro Ser Val Gln His Gly Gly Arg Pro Cys Glu Gly Asn Ala Val Glu Ile Ile Met Cys Asn Ile Arg Pro Cys Pro

Val His Gly Ala Trp Ser Ala Trp Gln Pro Trp Gly Thr Cys Ser Glu
770 780

Ser Cys Gly Lys Gly Thr Gln Thr Arg Ala Arg Leu Cys Asn Asn Pro 785 790 795 800

Pro Pro Ala Phe Gly Gly Ser Tyr Cys Asp Gly Ala Glu Thr Gln Met 805 810 815

Gln Val Cys Asn Glu Arg Asn Cys Pro Ile His Gly Lys Trp Ala Thr 820 825 830

- Trp Ala Ser Trp Ser Ala Cys Ser Val Ser Cys Gly Gly Ala Arg 835 840 845
- Gln Arg Thr Arg Gly Cys Ser Asp Pro Val Pro Gln Tyr Gly Gly Arg 850 855 860
- Lys Cys Glu Gly Ser Asp Val Gln Ser Asp Phe Cys Asn Ser Asp Pro 865 870 875 880
- Cys Pro Thr His Gly Asn Trp Ser Pro Trp Ser Gly Trp Gly Thr Cys 885 890 895
- Ser Arg Thr Cys Asn Gly Gly Gln Met Arg Arg Tyr Arg Thr Cys Asp 900 905 910
- Asn Pro Pro Pro Ser Asn Gly Gly Arg Ala Cys Gly Gly Pro Asp Ser 915 920 925
- Gln Ile Gln Arg Cys Asn Thr Asp Met Cys Pro Val Asp Gly Ser Trp 930 935 940
- Gly Ser Trp His Ser Trp Ser Gln Cys Ser Ala Ser Cys Gly Gly 945 950 955 960
- Glu Lys Thr Arg Lys Arg Leu Cys Asp His Pro Val Pro Val Lys Gly 965 970 975
- Gly Arg Pro Cys Pro Gly Asp Thr Thr Gln Val Thr Arg Cys Asn Val 980 985 990
- Gln Ala Cys Pro Gly Gly Pro Gln Arg Ala Arg Gly Ser Val Ile Gly 995 1000 1005
- Asn Ile Asn Asp Val Glu Phe Gly Ile Ala Phe Leu Asn Ala Thr 1010 1015 1020
- Ile Thr Asp Ser Pro Asn Ser Asp Thr Arg Ile Ile Arg Ala Lys 1025 1030 1035
- Ile Thr Asn Val Pro Arg Ser Leu Gly Ser Ala Met Arg Lys Ile 1040 1045 1050
- Val Ser Ile Leu Asn Pro Ile Tyr Trp Thr Thr Ala Lys Glu Ile

1055 1060 1065

Gly	Glu 1070	Ala	Val	Asn	Gly	Phe 1075	Thr	Leu	Thr	Asn	Ala 1080	Val	Phe	Lys
Arg	Glu 1085		Gln	Val	Glu	Phe 1090	Ala	Thr	Gly	Glu	Ile 1095	Leu	Gln	Met
Ser	His 1100	Ile	Ala	Arg	Gly	Leu 1105	Asp	Ser	Asp	Gly	Ser 1110	Leu	Leu	Leu
Asp	Ile 1115	Val	Val	Ser		Туг 1120	Val	Leu	Gln	Leu	Gln 1125	Ser	Pro	Ala
Glu	Val 1130		Val	Lys		Tyr 1135		Glu	Asp	Tyr	Ile 1140		Thr	Gly
Pro	Gly 1145	Gln	Leu	Tyr	Ala	Tyr 1150	Ser	Thr	Arg	Leu	Phe 1155	Thr	Ile	Asp
Gly	Ile 1160	Ser	Ile	Pro	Tyr	Thr 1165	Trp	Asn	His	Thr	Val 1170	Phe	Tyr	Asp
Gln	Ala 1175	Gln	Gly	Arg	Met	Pro 1180	Phe	Leu	Val	Glu	Thr 1185	Leu	His	Ala
Ser	Ser 1190	Val	Glu	Ser	Asp	Tyr 1195	Asn	Gln	Ile	Glu	Glu 1200	Thr	Leu	Gly
Phe	Lys 1205	Ile	His	Ala	Ser	Ile 1210	Ser	Lys	Gly	Asp	Arg 1215	Ser	Asn	Gln
Сув	Pro 1220	Ser	Gly	Phe	Thr	Leu 1225	Asp	Ser	Val	Gly	Pro 1230	Phe	Cys	Ala
Asp	Glu 1235	Asp	Glu	Cys	Ala	Ala 1240	Gly	Asn	Pro	Сув	Ser 1245	His	Ser	Сув
His	Asn 1250	Ala	Met	Gly	Thr	Tyr 1255	Tyr	Cys	Ser	Суз	Pro 1260	Lys	Gly	Leu
Thr	Ile 1265	Ala	Ala	Asp	Gly	Arg 1270	Thr	Cys	Gln	Asp	Ile 1275	Asp	Glu	Cys

Ala Leu Gly Arg His Thr Cys His Ala Gly Gln Asp Cys Asp Asn 1280 1285 1290

Thr Ile Gly Ser Tyr Arg Cys Val Val Arg Cys Gly Ser Gly Phe 1295 1300 1305

Arg Arg Thr Ser Asp Gly Leu Ser Cys Gln Asp Ile Asn Glu Cys 1310 1315 1320

Gln Glu Ser Ser Pro Val Thr Ser Ala Val Ser Met Pro 1325 1330 1335

<210> 34

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<212> DNA

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